UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,423	09/10/2003	Tammy Burd Mehta	100/03021	4629

21569 7590 02/16/2007

CALIPER LIFE SCIENCES, INC.
605 FAIRCHILD DRIVE
MOUNTAIN VIEW, CA 94043-2234

EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/659,423	MEHTA, TAMMY BURD	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/27/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-10 are pending. The following Office Action is in response to Applicant's response dated November 27, 2006.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claim(s) 1, 3-7, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stapleton (U.S. 5,188,963), in view of Moreira ("Efficient removal of PCR inhibitors using agarose-embedded DNA preparations" Nucleic Acids Research. 1998. Vol. 26, No. 13: Pages 3309-3310), in further view of Maniatis et al. *Molecular cloning: a laboratory Manual.* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1982): pages 150-152.

With regard to claim(s) 1 and 3, Stapleton discloses methods of samples to be analyzed for the presence of a particular DNA component comprising: (a) amplifying a

desired nucleic acid component in matrix material; and (b) applying an electric current to the matrix material (col. 3, lines 20-40, for example). Stapleton further discloses the matrix as being a semi-solid material made with agarose or acrylamide or similar polymer, or mixture thereof (col. 8, lines 40-65, for example). Stapleton further discloses that this research clearly demonstrates amplification in agarose gels by the Polymerase Chain Reaction (PCR) with Taq polymerase (Column 12, Lines 20-35, for example). Stapleton discloses several examples (Columns 14-18; especially Example 2) wherein PCR amplification followed by electrophoretic separation is performed within a "sieving matrix." Stapleton does not specifically disclose ranges of polymer concentration, however, Stapleton does disclose that the purpose of varying materials, *or the volume and concentration thereof,* in submatrix sections on the same carrier is to optimize conditions for a specific method (col. 9, lines 35-45, for example).

Moreira discloses that agarose-embedded DNA can be directly used for PCR since low melting point (LMP) agarose does not interfere with the reaction (Abstract). Moreira further discloses agarose-embedded DNA is useful for PCR, since reactions are not affected by the presence of high quality LMP agarose concentrations even as high as 0.3% in the PCR mixture (Page 3309, Column 2, End Paragraph 1).

Moreira clearly teaches PCR within agarose concentrations "even as high as 0.3%", however, Moreira teaches electrophoresis of PCR products on a 1.2% gel. It is submitted that that particular method step is **necessitated by the size of the PCR product**. Moreira teaches the amplification and resolving of a 0.6 kb and 0.85 kb fragment, which require that agarose gel concentration for efficient separation.

It was a well-known scientific fact at the time of invention (see Maniatis et al. *Molecular cloning: a laboratory Manual.* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1982): pages 150-152) that agarose gels having different polymer concentrations have different ranges of separation for linear DNA molecules. A larger amplification product (i.e. greater kb length **such as 60-5 kb**) requires polymer mixture of less concentration for accurate separation, **i.e. 0.3% agarose** (pg. 150).

It would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to incorporate an amplification and electrophoretic separation steps within agarose concentrations "even as high as 0.3%" since the combined references suggest such a modification for specific separation of linear DNA molecules of a larger size.

With regard to claim(s) 4 and 5, Stapleton discloses acrylamide or similar polymer, or mixture thereof (Column 8, Lines 40-65). It is noted that the Moreira reference discloses PCR in the presence of agarose only, however, Stapleton does disclose a polyacrylamide (Column 15, Lines 5-10, for example).

With regard to claim(s) 6, Stapleton discloses the matrix as being a semi-solid material made with agarose (Column 8, Lines 40-65).

With regard to claim(s) 7, Stapleton discloses PCR with Taq polymerase (Column 12, Lines 20-35, for example).

With regard to claim(s) 10, Stapleton discloses electrophoretic separation (Columns 14 and 15, Example 2, for example).

2. Claim(s) 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stapleton (U.S. 5,188,963) in view of Moreira ("Efficient removal of PCR inhibitors using agarose-embedded DNA preparations" Nucleic Acids Research. 1998. Vol. 26, No. 13: Pages 3309-3310), in further view of Maniatis et al. *Molecular cloning: a laboratory Manual.* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1982): pages 150-152, in further view of Woolley et al. "Ultra-high-speed DNA fragment separations using microfabricated capillary array electrophoresis chips" Proc. Natl. Acad. Sci. November 1994. Vol. 91: Pages 11348-11352).

With regard to claim(s) 8 and 9, the methods of Stapleton and Moreira have been outlined in the above rejections. Neither Stapleton nor Moreira specifically disclose methods within microfluidic channels.

Woolley et al. disclose mixing a PCR reaction component with a sieving matrix and subsequent electrophoretic separation within a microfluidic channel (Page 11349, Column 2, Electrophoresis Procedures; Figure 2, for example). From the teachings of Woolley, the particular advantages of microfluidic devices, such as significant reduction in space and reagent requirements, would have been clearly evident to a practitioner of ordinary skill in the art.

It would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to incorporate the methods of Stapleton into a microfluidic

device since Woolley suggests such a modification for, among other reasons, significant reduction in space and reagent requirements.

Response to Arguments - Claim Rejections - 35 USC § 103

Applicant's arguments with respect to the previously applied references have been fully considered but they are not persuasive.

Rejection of claim(s) 1 and 3-10 over Stapleton in view of Moreira and Maniatis

The crux of Applicant's arguments revolve around the assertion none of the applied references teach or suggest using the *same* sieving medium for thermocycling and separating. Applicant further directs the Examiner to specific sections of Stapleton and Moreira where they describe the amplification and separation matrices as being of different compositions and submits that this is evidence that the applied references teach away from the claimed invention.

Applicant's arguments are not persuasive because, as noted above, Moreira teaches the amplification and resolving of 0.6 kb and 0.85 kb fragments using an agarose concentration of 1.2%, which is was **common practice** at the time of invention (see Maniatis et al. *Molecular cloning: a laboratory Manual.* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1982): pages 150-152). Maniatis expressly teaches that 6-0.4 kb to be an efficient range of separation of linear DNA molecules for an agarose concentration of 1.2% (pg. 150). They further teach that **60-5 kb** to be an efficient range of separation of linear DNA molecules for an **agarose concentration of**

0.3% (pg. 150). Thus, a practitioner amplifying target molecules of such length by the methods suggested by Moreria, i.e. 60-5 kb, would have been motivated to use an agarose concentration of around 0.3% in the PCR reaction as well as the electrophoretic separation. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to practice PCR and subsequent separation within the **same sieving medium** having a polymer concentration of less than about 0.4%.

Rejection of claim(s) 1 and 3-10 over Stapleton in view of Moreira, Maniatis, and Woolley

Please see the response above.

Thus, the rejections are maintained.

Conclusion

Claims 1 and 3-10 are rejected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M. Babic
Patent Examiner
AU 1637

2-7-07

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

2/13/07